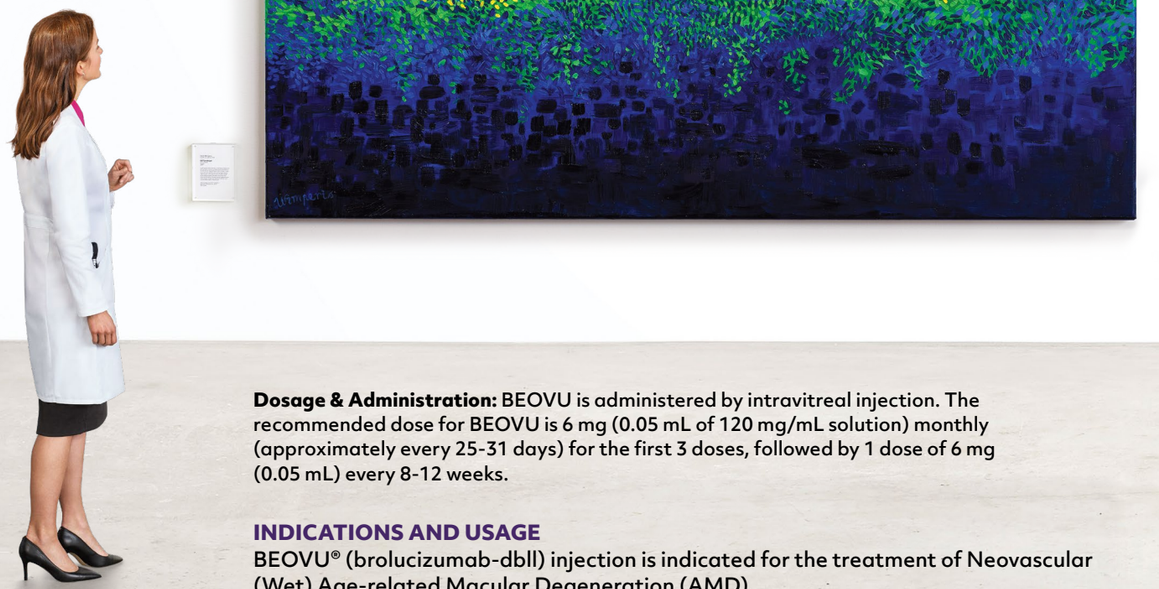
Beovu®
(brolucizumab-dbll)
Injection

THIS WAY TO
BEOVU DATA →



For patients with wet AMD[1]

THEIR VISION IS A WORK OF ART

In 2 head-to-head trials vs aflibercept, BEOVU[1,2]:

- **Achieved** similar mean change in BCVA at Week 48[1]*
- **Started** eligible patients on Q12 immediately after loading, and **maintained** over half at Week 48 (56% and 51%)[1,2†]
- **Demonstrated** greater CST reductions and fewer patients with IRF and/or SRF as early as Week 16, and at Week 48[2‡]

In HAWK, superior CST reductions and reductions in the percentage of patients with IRF and/or SRF were achieved at Week 16 and Week 48. In HARRIER, *P* values are nominal and not adjusted for multiplicity.[2] Clinical significance has not been established. No conclusions of efficacy may be drawn.

Study design: The safety and efficacy of BEOVU were assessed in 2 randomized, multicenter, double-masked, active-controlled, 2-year, Phase III studies in patients with wet AMD (N=1459). The primary endpoint demonstrated noninferiority in mean change in BCVA from baseline to Week 48 vs aflibercept as measured by ETDRS letters. Patients were randomized to either BEOVU 6 mg or aflibercept 2 mg (Q8 per label). Disease Activity Assessments (DAAs) were conducted throughout the trial at prespecified intervals. After 3 initial monthly doses, treating physicians decided whether to treat each patient on a Q8 or Q12 interval guided by visual and anatomical measures of disease activity, although the utility of these measures has not been established. Patients with disease activity at Week 16 or at any DAA could be adjusted to Q8 for the remainder of the study.[1,2]

Dosage & Administration: BEOVU is administered by intravitreal injection. The recommended dose for BEOVU is 6 mg (0.05 mL of 120 mg/mL solution) monthly (approximately every 25-31 days) for the first 3 doses, followed by 1 dose of 6 mg (0.05 mL) every 8-12 weeks.

INDICATIONS AND USAGE

BEOVU® (brolucizumab-dbll) injection is indicated for the treatment of Neovascular (Wet) Age-related Macular Degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or known hypersensitivity to brolucizumab or any of the excipients in BEOVU. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

AMD=age-related macular degeneration; BCVA=best corrected visual acuity; CST=central subfield thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; IRF=intraretinal fluid; Q8=treatment every 8 weeks; Q12=treatment every 12 weeks; SRF=subretinal fluid.

IMPORTANT SAFETY INFORMATION (CONT)

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachment

Intravitreal injections, including those with BEOVU, have been associated with endophthalmitis and retinal detachment. Proper aseptic injection techniques must always be used when administering BEOVU. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Retinal Vasculitis and/or Retinal Vascular Occlusion

Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of BEOVU. Patients should be instructed to report any change in vision without delay.

Please see additional Important Safety Information throughout and full Prescribing Information.

*The primary endpoint was to demonstrate efficacy in mean change in BCVA from baseline at Week 48, measured by ETDRS letters. BEOVU (Q8/Q12) demonstrated noninferiority in BCVA to aflibercept 2 mg (fixed Q8).[1]
†In HAWK and HARRIER, respectively. All remaining patients were on Q8. Patients on BEOVU could be adjusted from Q12 to Q8 at any disease activity assessment.[1,2]
‡CST reductions in patients on BEOVU vs aflibercept at Week 16 in HAWK (*P*=0.0008): -161.4 µm vs -133.6 µm; Week 48 (*P*=0.0012): -172.8 µm vs -143.7 µm. CST reductions in patients on BEOVU vs aflibercept at Week 16 in HARRIER (*P*<0.0001): -174.4 µm vs -134.2 µm; Week 48 (*P*<0.0001): -193.8 µm vs -143.9 µm. Percentage of patients with IRF and/or SRF on BEOVU vs aflibercept at Week 16 in HAWK (*P*<0.0001): 34% vs 52%; Week 48 (*P*=0.0001): 31% vs 45%. Percentage of patients with IRF and/or SRF on BEOVU vs aflibercept at Week 16 in HARRIER (*P*<0.0001): 29% vs 45%; Week 48 (*P*<0.0001): 26% vs 44%.[2-4]

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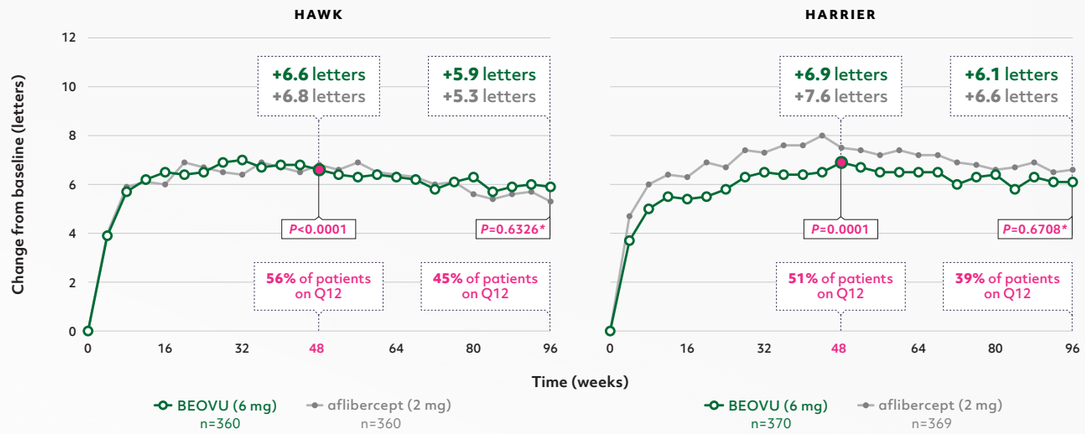
Achieved similar mean change in BCVA at Week 48[1]

Visual acuity gains observed at Week 48 were maintained at Week 96[1]

Mean change in BCVA with BEOVU vs aflibercept from baseline to Week 96[1,3,4]



The primary endpoint was to demonstrate efficacy in mean change in BCVA from baseline at Week 48, measured by ETDRS letters. Both studies confirmed the hypothesis of noninferiority at Week 48 with a margin of 4.0 letters.[1,2]

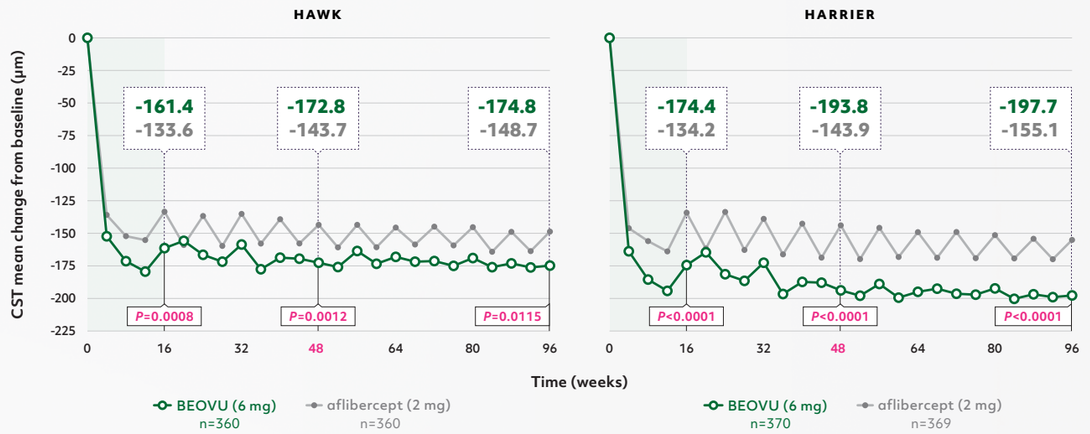
*Week 96 data for HAWK and HARRIER were descriptive only. Week 96 *P* values were not statistically significant.

RESULTS SEEN WITH
over half of patients on Q12 at Week 48 (56% and 51%)[1]
At Week 96, 45% and 39% of patients were on Q12[1]

Greater CST reductions[2]

BEOVU achieved greater reductions in CST vs aflibercept through Week 96[5,6]

Secondary endpoint: CST reductions with BEOVU vs aflibercept from baseline to Week 96[3-6]

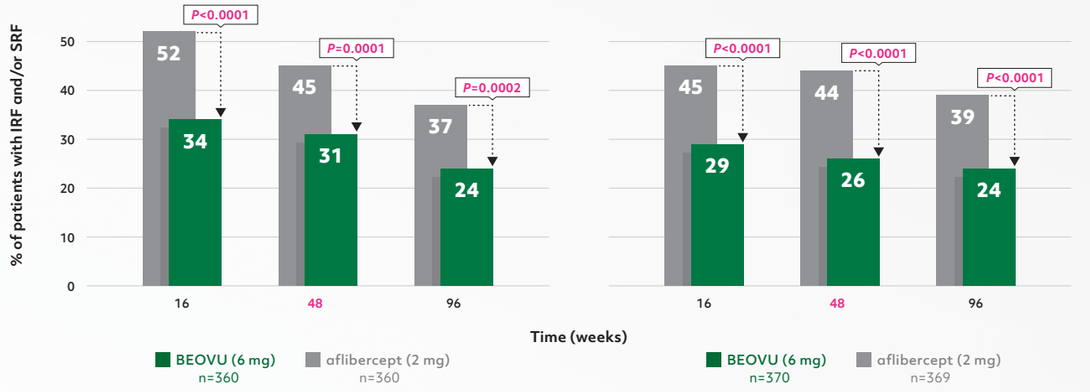


In HAWK, superior CST reductions were achieved at Week 16 and Week 48. In HARRIER, *P* values are nominal and not adjusted for multiplicity.[2] Week 96 data for HAWK and HARRIER were descriptive only. Clinical significance has not been established. No conclusions of efficacy may be drawn.

Fewer patients with IRF and/or SRF[2]

Fewer patients on BEOVU had IRF and/or SRF vs aflibercept through Week 96[6,7]

Secondary endpoint: % of patients on BEOVU with IRF and/or SRF vs aflibercept at Weeks 16, 48, and 96[3,4,6,7]



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IMPORTANT SAFETY INFORMATION (CONT)

WARNINGS AND PRECAUTIONS (CONT)

Increase in Intraocular Pressure

Acute increases in intraocular pressure (IOP) have been seen within 30 minutes of intravitreal injection including with BEOVU. Sustained IOP increases have also been reported. Both IOP and perfusion of the optic nerve head must be monitored and managed appropriately.

Thromboembolic Events

Although there was a low rate of arterial thromboembolic events (ATEs) observed in the BEOVU clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. Arterial thromboembolic events are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The ATE rate in the two controlled 96-week neovascular AMD studies (HAWK and HARRIER) during the first 96-weeks was 4.5% (33 of 730) in the pooled brolucizumab arms compared with 4.7% (34 of 729) in the pooled aflibercept arms.

ADVERSE REACTIONS

Serious adverse reactions including endophthalmitis, retinal detachment, retinal vasculitis and/or retinal vascular occlusion, increases in intraocular pressure, and arterial thromboembolic events have occurred following intravitreal injections with BEOVU.

The most common adverse events (≥5% of patients) with BEOVU were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain.

As with all therapeutic proteins, there is a potential for an immune response in patients treated with BEOVU. Anti-brolucizumab antibodies were detected in the pre-treatment sample of 36% to 52% of treatment naive patients. After initiation of dosing, anti-brolucizumab antibodies were detected in at least one serum sample in 53% to 67% of patients treated with BEOVU. Intraocular inflammation was observed in 6% of patients with anti-brolucizumab antibodies detected during dosing with BEOVU. The significance of anti-brolucizumab antibodies on the clinical effectiveness and safety of BEOVU is not known.

INDICATIONS AND USAGE

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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Beovu® (brolucizumab-dbll) Injection

Clinical safety profile

Common adverse reactions (≥1%) in HAWK and HARRIER (pooled data) through Week 96[1]

Adverse Drug Reactions	BEOVU (N=730)	Active Control (aflibercept) (N=729)
Vision blurred*	10%	11%
Cataract	7%	11%
Conjunctival hemorrhage	6%	7%
Vitreous floaters	5%	3%
Eye pain	5%	6%
Intraocular inflammation†	4%	1%
Intraocular pressure increased	4%	5%
Retinal hemorrhage	4%	3%
Vitreous detachment	4%	3%
Conjunctivitis	3%	2%
Retinal pigment epithelial tear	3%	1%
Corneal abrasion	2%	2%

Adverse Drug Reactions	BEOVU (N=730)	Active Control (aflibercept) (N=729)
Hypersensitivity‡	2%	1%
Punctate keratitis	1%	2%
Retinal tear	1%	1%
Endophthalmitis	1%	<1%
Blindness§	1%	<1%
Retinal artery occlusion	1%	<1%
Retinal detachment	1%	<1%
Conjunctival hyperemia	1%	1%
Lacrimation increased	1%	1%
Abnormal sensation in eye	1%	2%
Detachment of retinal pigment epithelium	1%	<1%

*Including vision blurred, visual acuity reduced, visual acuity reduced transiently, and visual impairment.[1]
†Including anterior chamber cell, anterior chamber flare, anterior chamber inflammation, chorioretinitis, eye inflammation, iridocyclitis, iritis, retinal vasculitis, retinal vascular occlusion, uveitis, vitreous haze, vitritis.[1]
‡Including urticaria, rash, pruritus, erythema.[1]
§Including blindness, blindness transient, amaurosis, and amaurosis fugax.[1]

- In HAWK, 3.1% of patients in the BEOVU arm discontinued due to ocular adverse events vs 3.3% for aflibercept[3]
- In HARRIER, 3.5% of patients in the BEOVU arm discontinued due to ocular adverse events vs 1.6% for aflibercept[4]

Patient monitoring and counseling‖

BEOVU is contraindicated in[1]:

- Patients with ocular or periocular infections
- Patients with active intraocular inflammation
- Patients with known hypersensitivity to brolucizumab or any of the excipients in BEOVU
  - Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation

Guidance[1]:

- Advise patients there is a risk of developing endophthalmitis, retinal detachment, retinal vasculitis, and/or retinal vascular occlusion in the days following BEOVU administration
  - Reports of retinal vasculitis and/or retinal vascular occlusion typically occurred in the presence of intraocular inflammation
- Patients should be monitored for increased intraocular pressure immediately following the intravitreal injection. Monitoring may include checking for perfusion of the optic nerve head or tonometry

Patients should be instructed to seek immediate care from their ophthalmologist if they experience any of the following symptoms or any change in vision[1]:

- Increased light sensitivity
- Floaters
- Pain in their eye
- Decrease in vision
- Redness on the white part of the eye

‖This is a subset of information from the Prescribing Information. As always, please review the full Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT)

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Please see additional Important Safety Information throughout and full Prescribing Information.

REFERENCES: 1. Beovu [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2020. **2.** Dugel PU, Koh A, Ogura Y, et al, on behalf of the HAWK and HARRIER Study Investigators. HAWK and HARRIER: Phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. *Ophthalmology*. 2020;127(1):72-84. **3.** Data on file. RTH258-C001 Clinical Study Report. Novartis Pharmaceuticals Corp; December 2018. **4.** Data on file. RTH258-C002 Clinical Study Report. Novartis Pharmaceuticals Corp; December 2018. **5.** Data on file. RTH258-C001 & RTH258-C002 CST. Novartis Pharmaceuticals Corp; September 2019. **6.** Dugel PU, Singh RP, Koh A, et al. HAWK and HARRIER: Ninety-six-week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration. *Ophthalmology*. 2020. doi:10.1016/j.ophtha.2020.06.028. **7.** Data on file. RTH258-C001 & RTH258-C002 IRF and/or SRF. Novartis Pharmaceuticals Corp; October 2019.

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